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Running Title: Silica-induced inflammatory mediators

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Abbreviations:

AM - alveolar macrophage, BAL - bronchoalveolar lavage, ELISA - enzyme-linked immunoassays, GM-CSF - granulocyte/macrophage-colony stimulating factor, iNOS - inducible nitric oxide synthase, ICAM-1 - intercellular adhesion molecule-1, IL – interleukin, MIP-2 - macrophage inflammatory protein-2, MCP-1 - monocyte chemoattractant protein-1, PMN – polymorphonuclear neutrophils, TGF -transforming growth factor, TNF-α - tumor necrosis factor-α, type II cells - alveolar epithelial type II cells.

Abstract

The expression of 10 genes implicated in regulation of the inflammatory processes in the lung was studied following exposure of alveolar macrophages (AM) to silica *in vitro* or *in vivo*. Exposure of AM to silica *in vitro* upregulated the mRNA levels of three genes (IL-6, MCP-1, and MIP-2) without a concomitant increase in the protein levels. AM isolated following intratracheal instillation of silica upregulated mRNA levels of four additional genes (GM-CSF, IL-1β, IL-10 and iNOS). Protein levels IL-6, MCP-1 and MIP-2 were elevated in bronchoalveolar lavage (BAL) fluid. Fibroblasts under basal culture conditions express much higher levels of IL-6 and GM-CSF compared to AM. Co-culture of AM and alveolar type II cells, or co-culture of AM and lung fibroblasts, in contact cultures or Transwell chambers, revealed no synergistic effect. Therefore, such interaction does not explain the effects seen *in vivo*. In conclusion, identification of the intercellular communication *in vivo* is still unresolved. However, fibroblasts appear to be an important source of inflammatory mediators in the lung.